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PART III

ENVIRONMENTAL PROTECTION AGENCY

RESPONSE TO INTERAGENCY TESTING COMMITTEE RECOMMENDATIONS

[6560-01-M]

ENVIRONMENTAL PROTECTION AGENCY

[FRL 989-5]

RESPONSE TO INTERAGENCY TESTING COMMITTEE RECOMMENDATIONS

AGENCY: Environmental Protection Agency.

ACTION: Notice in response to Interagency Testing Committee recommendations.

SUMMARY: Section 4(e) of the Toxic Substances Control Act (TSCA) (90 Stat 2003, 15 U.S.C. 2601 et seq.) established an Interagency Testing Committee (ITC) to recommend to the Administrator of the Environmental Protection Agency (EPA) a priority list of chemicals to be considered for testing. TSCA requires EPA to respond to these recommendations within 1 year, either by initiating rulemaking proceedings under section 4(a) or by publishing in the FEDERAL REGISTER EPA's reasons for not taking this action.

On October 4, 1977, the ITC transmitted its initial priority list of recommendations to EPA. The Agency has initiated review and evaluation of the October 1977 recommendations. However, for the reasons discussed in this notice, EPA is not initiating section 4(a) rulemaking proceedings for these recommendations at this time.

FOR FURTHER INFORMATION CONTACT

John B. Ritch, Jr., Director, Industry Assistance Office, Office of Toxic Substances (TS-799), Environmental Protection Agency, 401 M Street SW., Washington, D.C. 20460, 800-424-9065; in Washington, D.C. call 554-1404.

SUPPLEMENTARY INFORMATION:

BACKGROUND

TSCA established the ITC to recommend to the Administrator of EPA chemical substances and mixtures [1] for priority attention in developing test rules under section 4(a) of TSCA. The Act required the ITC to transmit its initial priority list to the Administrator by October 3, 1977, and to consider updating that list at least every 6 months thereafter.

The ITC's initial priority list of four individual chemicals and six categories of chemicals was transmitted to EPA on October 4, 1977, and subsequently published in the FEDERAL REGISTER (42 FR 55026, Oct. 12, 1977). As permitted by section 4(e)(1)(A) of TSCA, each of the 10 chemicals on the October 1977 priority list was designated for special consideration by EPA within 12 months. As a result, the Agency must respond to the ITC's recommendations within the 12-month period either by initiating a rulemaking action or by publishing EPA's reasons for not doing so. Although the ITC subsequently added other designated chemicals to the priority list (43 FR 16684, April 19, 1978), at this time the Agency is only required to respond to the recommendations on the October 1977 priority list. Those recommendations are summarized in the following table:

Substance or category	Testing recommended
Alkyl epoxides	Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, and epidemiological study.
Alkyl phthalates	Environmental effects.
Chlorinated benzenes, mono- and di-.	Carcinogenicity, mutagenicity teratogenicity, other chronic effects, environmental effects and epidemiological study.
Chlorinated paraffins.	Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and environmental effects.
Chloromethane	Carcinogenicity, mutagenicity, teratogenicity, and other chronic effects.
Cresols	Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and environmental effects.
Hexachloro-1,3-butadiene.	Environmental effects.
Nitrobenzene	Carcinogenicity, mutagenicity, and environmental effects.
Toluene	Carcinogenicity, teratogenicity, other chronic effects, and epidemiological study.
Xylenes	Mutagenicity, teratogenicity, and epidemiological study.

EPA plans to propose standards for oncogenicity and chronic effects testing by late December 1978 and to propose chemicals to be tested for these effects shortly thereafter. In addition, development of test standards for several other effects is in progress.

STATEMENT OF REASONS

Within 1 year of a chemical's designation by the ITC, EPA must either initiate a rulemaking proceeding to require testing or publish the Agency's reasons for not doing so.

The Act does not specify which of several possible EPA actions would initiate a rulemaking proceeding for purposes of section 4(e). However, as a matter of policy, EPA plans to equate "initiating a rulemaking proceeding" with proposing a section 4(a) rule. For the reasons discussed below, the Agency is not initiating rulemaking at this time.

Before proposing section 4 test rules fof the chemicals the ITC recommended, the Agency must review available information on those chemicals according to the statutory prerequisites for testing prescribed by TSCA section 4(a). In addition, the Agency must prescribe appropriate standards for the conduct of the tests it requires. Although work is progressing on these facets of the rulemaking decision for the chemicals the ITC recommended, neither activity has been completed.

The findings required by section 4(a) to propose a test rule demand substantially more detailed information and evaluation than is required of the ITC in making its recommendations under section 4(e). For example, while the ITC may recommend a chemical without considering on-going studies, EPA must decide whether such studies are likely to provide adequate data for assessing risk before making section 4(a) findings.

EPA's evaluation of the ITC's recommendations, which is still in progress, includes review of (1) The ITC dossiers and their references, (2) studies and reports identified by an EPA supplementary literature search, and (3) the public comments in response to publication of the priority list in the FEDERAL REGISTER. Furthermore, EPA has promulgated a section 8(d) rule requiring the submission of unpublished health and safety studies for the Agency's use in its review of these chemicals (43 FR 30984, July 18, 1978). Those studies are still being received and will be evaluated before test rules are proposed.

In addition to this full review of the chemicals recommended by the ITC, EPA generally plans to prescribe test methodologies as a part of its test rules to insure that the test data will be reliable and meet the Agency's needs. Proposing specific test methods also should aid the public in commenting on the testing that EPA considers necessary to assess the risk of these chemicals. The test standards needed to implement the ITC's recommendations have not yet been completed.

Finally, proposing the first test rules under TSCA requires resolution of several basic scientific and policy questions. For example, decisions have to be made on when to test pure substances and when to require testing of commercial grades of chemicals that may contain byproducts, impurities, and additives. EPA has not yet completed its consideration of this and other issues related to section 4 rulemaking.

STATUS OF EPA'S EVALUATION

On the basis of its review thus far (as summarized in the Appendix to this Notice), EPA concludes that each of the 10 chemicals on the initial Pri-

[1] TSCA's language is "chemical substance or mixture"; in 42 FR 55026, the ITC uses "substances and categories." The term "chemical(s)" is used in this notice to avoid confusion.

ority List should continue to be considered for section 4(a) rulemaking.

Although the Agency considers publication of this Notice to remove the priority designation of the 10 chemicals on the October 1977 Priority List,[2] the chemicals retain high priority within EPA for further section 4(a) consideration. As the Agency's evaluation of the chemicals and its development of test standards are completed, EPA will propose test rules[3] for each of the chemicals and effects designated by the ITC that meet the requirements of section 4(a). Where EPA finds that existing information does not support the need for a test rule, the Agency will publish a Notice in the FEDERAL REGISTER stating in detail its reasons for not requiring testing.

Dated: October 10, 1978.

BARBARA BLUM,
Acting Administrator.

APPENDIX—EPA'S PRELIMINARY APPRAISAL OF THE ITC'S OCTOBER 1977 RECOMMENDATIONS

EPA's preliminary appraisals of the ITC's October 1977 recommendations are presented in this Appendix. In general, EPA feels that the testing recommended by the ITC for these chemicals seems appropriate. However, the Agency has not yet completed its evaluation of the recommendations or determined whether testing regulations for these chemicals should be proposed under section 4(a) of TSCA.

ALKYL EPOXIDES

The alkyl epoxides category includes all noncyclic aliphatic hydrocarbons with one or more epoxy functional groups. The ITC has recommended testing for carcinogenicity, mutagenicity, teratogenicity, and other chronic effects because the epoxy structure is a relatively reactive functional group that is believed to be the source of the carcinogenic and mutagenic activity already well characterized for several members of the category. Although the alkyl epoxides are generally used as intermediates, the ITC noted that the large production volumes of some members raise concern with respect to workplace exposure. The ITC recommended retrospective epidemiologic studies for the members with the highest exposure. The ITC also recommended environmental effects testing, expressing particular concern for alkyl epoxide reaction products.

SUPPLEMENTAL LITERATURE SEARCH

The ITC dossier did not report that EPA has published a notice of Rebuttable Presumption Against Registration for ethylene oxide, nor that the FDA has published a notice of intent to establish maximum residue limits for ethylene oxide and its major reaction products in drug products and medical devices and to establish maximum daily exposure levels from these items. EPA will consider this information in further evaluating the need for testing of ethylene oxide.

Only one study was found in the supplemental literature search that appeared to be pertinent to the ITC recommendations. Joyner (1964)[4] reported on the health records of 37 employees of an ethylene oxide manufacturing plant. This study will be further evaluated, with particular attention given to its relevance to the ITC recommendation for epidemiologic study.

PUBLIC COMMENTS

Comment 1: The estimated environmental release figures were questioned. The ITC dossier reports estimated annual environmental release rates of 98.8 million pounds for ethylene oxide and 40.8 million pounds for propylene oxide. For ethylene oxide, one commentor estimated that the total annual environmental release is less than 20 million pounds; another commentor placed it at 10–12 million pounds. For propylene oxide, one commentor estimated that less than 5 million pounds is released to the environment annually.

Response 1: The environmental release rate data presented in the ITC dossier are from the report "A Study of Industrial Data on Candidate Chemicals for Testing, Research Request No. 1" (EPA 560/5-77-006, August 1977) and reflect the application of estimated production-loss factors and dispersive-use factors to production and consumption of these compounds. These factors may overestimate the environmental losses of ethylene oxide and propylene oxide. Additional evaluation of environmental release data will be nesessary in developing any test rules for these compounds.

Comment 2: The occupational exposure population sizes presented in the dossier are overestimated.

Response 2: The NIOSH/NOHS data used in the dossier indicate that 165,000 and 264,000 persons are exposed occupationally to ethylene oxide and propylene oxide, respectively. The commentors' estimates of 110,000 to 115,000 for ethylene oxide do no differ greatly from the NOHS data; however, the commentors' estimates of 5000 to 8000 persons exposed occupationally to propylene oxide differ substantially from the NOHS data. Additional evaluation of the propylene oxide exposure potential will be necessary in developing any test rules.

Comment 3: The category name "alkyl epoxides" inaccurately defines the group of compounds in question because it does not, technically, include ethylene oxide. The commentor offers oxiranes, epoxyalkanes, alkylene oxides, and epoxides as alternatives.

Response 3: The commentor is correct. Technically, the category "alkyl epoxides" does not include ethylene oxide. The suggested alternatives "oxiranes" and "epoxides" describe a much larger class of compounds than intended. "Epoxy alkanes" and "alkylene oxides" both appear to be suitable alternatives and will be considered in developing any test rules for this class of compounds.

Note on Comments 4-7: These comments address specific alkyl epoxides for which ongoing studies or available data may obviate the need for testing requirements. EPA recognizes, as did the ITC, that certain members of a recommended category may already have been adequately tested for one or more of the effects of concern. In developing test rules, these cases will be examined in detail and, where available data (or tests in progress) are considered adequate, testing will not be required.

Comment 4: Studies are presently being conducted at the Carnegie–Mellon Institute that will provide an adequate characterization of the carcinogenicity, mutagenicity, teratogenicity, and other chronic effects of ethylene oxide, and therefore testing requirements for these effects are not necessary.

Response 4: The ITC was aware of these studies when making its recommendations. EPA will review in detail the protocols and any results from these studies when developing test rules for alkyl epoxides. If the effects of ethylene oxide are adequately determined in these studies, no further testing of ethylene oxide will be required for these effects.

Comment 5: Long-term studies planned at the Central Institute for Nutrition and Food Research will adequately characterize the carcinogenicity and other chronic effects of propylene oxide. Testing requirements for these effects will not be nesessary.

Response 5: It will be necessary for EPA to obtain the full protocols being employed in these studies in order to determine the adequacy of these tests. In further considering test rules EPA will evaluate the protocols and whatever preliminary results are available.

Comment 6: The mutagenicity and teratogenicity studies being conducted on ethylene oxide will serve as indicators of the need for testing propylene oxide for these effects.

Response 6: The results of the mutagenicity and teratogenicity studies on ethylene oxide will not be a strong factor in determining the need to test propylene oxide for these effects. It is well known that there can be vast differences between the effects of the first two members of an homologous series (e.g., methanol and ethanol).

Comment 7: Adequate data are available on the health and environmental effects of butylene oxide. Because of this and its low human and envoronmental exposure potential, testing requirements for butylene oxide are unnecessary.

Response 7: The available health and environmental effects data, as well as exposure aspects, will be considered in detail when considering any testing requirements for butylene oxide.

Comment 8: Epidemiological studies of ethylene oxide and propylene oxide in certain production and processing plants are unnecessary and impractical because medical surveillance indicates no unusual medical problems among employees; these employees do not constitute a suitable cohort, and surveys show ambient levels consistently within the TLV.

Response 8: The experience of these commentors will be useful in examining the need for and feasibility of epidemiological study of these, and perhaps other, alkyl epoxides. EPA will utilize whatever information is available on such workplace experience in considering epidemiological study testing requirements.

Comment 9: The alkyl epoxides will react to form glycols which are relatively non-

[2] That is, that they no longer occupy 10 of the 50 places on the Priority List reserved for chemicals designated for action by EPA within 12 months. However, the ITC may redesignate any of these chemicals if it so chooses.

[3] EPA expects to issue separate rules for various effects as the appropriate test standards are completed.

[4] Arch. Environ. Hlth. *8*(5):700-710.

toxic, are rapidly biodegradable and do not bioaccumulate; any chlorohydrins formed would probably not persist. Further testing for environmental effects is unnecessary.

Response 9: Preliminary evaluation of the available literature indicates some merit in this comment. However, it does not appear that there are definitive data available on the formation and degradation of chlorohydrins, and testing may be necessary to determine if chlorohydrins from alkyl epoxides are an environmental concern.

PRELIMINARY APPRAISAL

The testing recommended by the ITC for this category of chemicals seems appropriate. However, further evaluation of ongoing, planned, and completed studies on specific alkyl epoxides (particularly on ethylene oxide and propylene oxide at Carnegie-Mellon Institute and the Central Institute for Nutrition and Food Research, respectively) will be necessary. Some of the recommended testing for certain members of the alkyl epoxides category may not be necessary if available data or studies in progress or planned are adequate. EPA will consider as alternative names for this category "epoxy alkanes" and "alkylene oxides".

ALKYL PHTHALATES (ALKYL ESTERS OF 1,2-BENZENEDICARBOXYLIC ACID)

The ITC recommended that all high production (e.g., 10 million lb/year or greater) alkyl phthalates be tested for environmental effects. This recommendation was based mainly on indications of their potential for environmental release, especially to the aquatic environment, on their environmental stability, and on the apparent toxicity of some phthalates to aquatic organisms.

SUPPLEMENTAL LITERATURE SEARCH

As a supplement to the ITC dossier, EPA has reviewed the information in the report "A Study of Industrial Data on Candidate Chemicals for Testing, Research Request No. 3" (EPA 560/5-78-002, June 1978). This document appeared to be more complete and more detailed than the ITC dossier. However, no studies were discussed in this report that suggest that the ITC's testing recommendations should be modified.

PUBLIC COMMENTS

Comment 1: The term "alkyl phthalates" inaccurately describes the class of compounds that the ITC is recommending for study. The term "dialkyl phthalates" is more accurate.

Response 1: EPA accepts this comment. It is clear that the ITC is in fact concerned with the dialkyl phthalates, and that its interest in monoalkyl phthalates is limited to their occurrence as metabolic or chemical degradation products of the dialkyl phthalates.

Comment 2: A distinction should be made between alkyl phthalates having an alkyl chain length of six or fewer carbon atoms and those with a chain length of more than six carbons.

Response 2: The implication of the comment is that the long-chain-length esters need not be tested for aquatic effects because they are insoluble in water and would float on the surface. Why these factors would make the long-chain alkyl phthalates devoid of aquatic effects worthy of concern was not substantiated by the commentor.

The ITC dossier cites studies showing that diethyhexyl phthalate (a long-chain ester) in water was found to affect the reproduction of the waterflea *Daphnia magna.*

Although at some point in the development of test rules it may be advantageous to make a distinction between alkyl phthalates of different chain lengths for specific testing requirements, there is no reason to make any distinction at this stage in considering the ITC recommendations.

Comment 3: There are inconsistencies between the production figures and the environmental release rates presented in the dossier. The release rate given for bis(2-ethylhexyl) phthalate is about 1.5 times the 1976 production value, and the release rate given for dibutyl phthalate is more than twice its 1976 production.

Response 3: The environmental release rates cited in the dossier are based on 1972 production data from the U.S. International Trade Commission. It is not appropriate to compare these release rates to 1976 production figures. The environmental release rates are consistent with the 1972 production data.

Comment 4: On-going and planned environmental studies at the University of Missouri on the alkyl phthalates make a testing rule unnecessary at this time.

Response 4: As test standards are developed for environmental effects testing, it will be possible to evaluate in detail the protocols being used in on-going and planned studies to determine whether they (and any results available from any of these studies) obviate the need for further testing. It is important to note that adequate environmental effects testing for one or more specific alkyl phthalates does not necessarily preclude the need for environmental effects testing of other alkyl phthalates.

PRELIMINARY APPRAISAL

The ITC's recommendation that all high production alkyl phthalates be tested for environmental effects seems appropriate. Additional evaluation of on-going and planned studies at the University of Missouri will be necessary to help determine whether specific tests for certain members are necessary.

EPA is also considering renaming this category "dialkyl phthalates," which is a more accurate description.

CHLORINATED BENZENES, MONO- AND DI-

This category, which consists of four structurally-related chemical substances, was recommended by the ITC for carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, and epidemiologic studies. The large production, widespread use, high release rate, and suspected persistence of the chlorinated benzenes were the primary considerations of the ITC in making these recommendations.

SUPPLEMENTAL LITERATURE SEARCH

Several articles were identified in the supplemental literature search which indicate that *p*-dichlorobenzene is mutagenic.[1] One study indicated that chlorobenzene is mutagenic[2] while another reported that it is not mutagenic.[3] Although on preliminary review these studies do not appear to have any impact on the ITC recommendation, they will be examined in more detail in considering mutagenicity testing requirements for these compounds.

With respect to environmental effects, a study was found which indicated that *o*-dichlorobenzene is lethal to phytoplankton at 1.3 p.p.m.;[4] another study showed that at 10 p.p.m. *o*-dichlorobenzene is comparatively harmless to clam larvae.[5] These studies do not suggest that environmental effects testing for *o*-dichlorobenzene is not needed, but they will aid in the design of any environmental effects testing scheme for this compound and, perhaps, for chlorinated benzenes as a category.

PUBLIC COMMENTS

Comment 1: Reasonable occupational exposure estimates are 10,000 persons for chlorobenzene and *o*-dichlorobenzene, and 5,000 persons for *p*-dichlorobenzene. The ITC dossier uses NIOSH/NOHS estimates of occupationally exposed populations of 1,093,000 persons for chlorobenzene, 1,978,000 persons for *o*-dichlorobenzene, and 540,000 persons for *p*-dichlorobenzene.

Response 1: Additional evaluation of the NOHS data base will be necessary to determine how well it defines the size of the occupationally exposed population. The commentor does not present any details on the basis for his estimates; these details will be sought and reviewed by EPA in considering these substances for testing.

Comment 2: m-Dichlorobenzene should be eliminated from consideration as a testing candidate because its production, environmental release, and exposure potential are low.

Response 2: While *m*-dichlorobenzene does appear to have the lowest exposure potential among the chlorinated benzenes, it has been detected in environmental samples (ground water, contaminated raw water, and drinking water). Whether or not exposure to *m*-dichlorobenzene is sufficiently low to obviate testing still needs to be determined.

Comment 3: On-going studies at the ICI Central Toxicology Laboratory will adequately characterize the mutagenicity, carcinogenicity, teratogenicity, and other chronic effects of *p*-dichlorobenzene, and therefore further testing is unnecessary. A proposed MCA study on the teratogenicity of chlorobenzene, *o*-dichlorobenzene, and *p*-dichlorobenzene makes a testing requirement for teratogenicity unnecessary.

Response 3: EPA will review in detail the protocols and any results from these planned and on-going studies when developing test rules. To the extent that these studies adequately characterize the effects of these substances, additional testing will not be required.

Comment 4: One producer commented that epidemiological study of chlorobenzene would not be necessary nor productive at his production site. This is based on having observed no unusual medical effects attributable to chlorobenzene exposure within the

[1] Sharma and Sakar (1957), Proc. Indian Acad. Sci., 45(B):288-293; Sharma and Bhattacharyya (1956), Cytologia, 21(4):353-360; Srivastava (1956), Cytologia, 31:166-171; Prasad and Pramer (1968), Genetics, 60:212-213.

[2] Prasad and Pramer (1968), Genetics, 60:212-213.

[3] Lyon (1975), Diss. Abstr., Int. B., 36:5537.

[4] Ukeles (1962), Appl. Microbiol., 10:532-537.

[5] Davis (1961), Comm. Fish. Rev., 23(12):8-23.

TLV's and because job mobility and workgroup size makes his employees an unsuitable cohort.

Response 4: The experience of this commentor may be useful in examining the need for and feasibility of epidemiological study of the chlorobenzenes. EPA will utilize whatever information is available on such workplace experiences in considering epidemiological study testing requirements.

Comment 5: One commentor provided information on photodegradation, rates of volatilization from water, biodegradibility, and bioaccumulation potential of mono- and dichlorobenzenes. The commentor indicates that although the chlorobenzenes are released to the environment in large amounts, the compounds do not present an unreasonable risk, and therefore testing should not be required.

Response 5: The data presented by this commentor do not appear to provide a sufficient basis for precluding further consideration of environmental effects testing.

PRELIMINARY APPRAISAL

The testing recommended by the ITC on these chemicals seems generally appropriate, a possible exception being the recommendations for testing of *m*-dichlorobenzene. Because the exposure potential for *m*-dichlorobenzene appears to be lower than those of monochlorobenzene, *o*-dichlorobenzene, and *p*-dichlorobenzene, further investigation of the exposure and environmental release sources of *m*-dichlorobenzene is necessary to help determine whether testing this substance is warranted.

Also, studies in progress at the ICI Central Toxicology Laboratory on *p*-dichlorobenzene and proposed studies by the Manufacturing Chemists Association on monochlorobenzene, *o*-dichlorobenzene and *p*-dichlorobenzene need to be evaluated to determine whether they will be adequate to assess the risks of exposure to these compounds.

CHLORINATED PARAFFINS

This category is comprised of mixtures of the chlorination products of materials known commercially as paraffin oils or paraffin waxes, limited to those having a chlorine content of 35 percent through 64 percent by weight. These compounds were recommended by the ITC for carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and environmental effects testing. The large environmental release rate, their use in a wide variety of household and paint products, and the occurrence of residues in fish formed the rationale for the ITC recommendations.

Although some additional information was found in the supplemental literature search on the uptake of chlorinated paraffins from water, on neurotoxic effects in fish, and on acute mammalian toxicity, this information does not eliminate the testing needs identified by the ITC.

No comments were received on the ITC's testing recommendations for chlorinated paraffins.

PRELIMINARY APPRAISAL

The testing recommended by the ITC seems appropriate. Some additional consideration needs to be given to the definition of this category of substances. EPA is considering increasing the upper limit on chlorine content to 70 percent by weight because this is the maximum percentage attainable in practice and because the ITC dossier refers to a study on a product of this composition.

CHLOROMETHANE

The ITC recommended that carcinogenicity, mutagenicity, teratogenicity, and other chronic effects testing be required for chloromethane. Though it is used primarily as an intermediate, annual environmental release (over 15 million pounds) and the number of workers exposed (about 31,000) were considered significant by the ITC.

No significant new information was identified in the literature search performed on chloromethane.

One comment indicated that a testing program has been initiated at the Chemical Industry Institute of Toxicology to study the carcinogenicity, teratogenicity, mutagenicity, and other chronic effects of chloromethane in response to the ITC's recommendations.

EPA will review the protocols of these studies, and any available results, in detail and determine if these studies will adequately characterize these effects of chloromethane.

PRELIMINARY APPRAISAL

The testing recommended by the ITC seems appropriate. The studies initiated at the Chemical Industry Institute of Toxicology on chloromethane need to be evaluated to determine whether test rules are necessary.

CRESOLS

The ITC recommended that cresols be tested for carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and environmental effects. These recommendations were based largely on information indicating significant environmental, occupational, and general population exposure, as well as on testing in these areas having been inadequate.

SUPPLEMENTAL LITERATURE SEARCH

The major data sources reviewed as supplemental to the ITC dossier are an SRI report entitled "A Study of Industrial Data on Candidate Chemicals for Testing, Research Request No. 3" (EPA 560/5-78-002, June 1978) and the NIOSH "Criteria for a Recommended Standard-Occupational Exposure to Cresol" (DHEW Publication No. 78-13, February 1978). Some additional information was found in these documents regarding the uses of cresols and their chronic toxicity, environmental fate, and ecological toxicity.

PUBLIC COMMENTS

Comment 1: The dossier presents misleading information concerning creosote oil as a source of cresols. The coal tar distillate presently called creosote oil is not the same as the coal tar distillate known historically as creosote oil. Modern day creosote oil contains very little cresols, and therefore creosote oil (used in wood preservation) is not a source of cresols to the environment.

The non-intermediate, potentially dispersive uses of cresols account for only a small fraction of the approximately 100 million pounds per year of production; the environmental release of cresols is on the order of 3 to 5 million pounds per year, not 30-45 million pounds.

Response 1: EPA agrees that creosote oil is chemically an ill-defined material and that the term has been applied to quite different materials, some of which may indeed have little or no cresols present in them.

With respect to the environmental release associated with the use pattern of cresols, no additional clarifying information has yet been found in the literature.

Additional investigation of creosote oil as a source of cresols to the environment, as well as further investigation into the use pattern of cresols, will be necessary in considering test rules for cresols, perhaps most importantly with regard to the environmental effects testing.

Comment 2: The ITC dossier states that approximately 2 million persons (referenced to the NIOSH/NOHS data base) are occupationally exposed to cresols; NIOSH estimates the exposed population at 11,000; one producer estimates the exposed population at 40,000; and another producer estimates the exposed population at about 670,000.

Response 2: It is not clear how the figure of 2 million was arrived at in the NOHS study, and NIOSH does not indicate in its Criteria Document why its estimate of 11,000 differs so dramatically from the NOHS estimate. NIOSH does state that its estimate of 11,000 is low because it does not include workers exposed intermittently to cresol-containing degreasing agents. (The estimate of 670,000 included 627,000 such workers.)

Some additional effort is needed to define more clearly the size and nature of the population exposed occupationally to cresols. However, NIOSH also stated the need for cresols to be studied for long-term, low-level exposure effects, carcinogenicity, mutagenicity, and teratogenicity.

PRELIMINARY APPRAISAL

The basis for the ITC's testing recommendations for cresols included information indicating a high potential for enviromental release and human exposure. The ITC's recommendations to test for carcinogenicity, mutagenicity, teratogenicity, chronic toxicity, and environmental effects seem appropriate if substantial exposure to cresols occurs. However, the extent of exposure to cresols needs to be further evaluated. Specifically, EPA's preliminary review has found that the use pattern of cresols suggests a substantially lower environmental release rate than that cited in the ITC dossier. In addition, the occupationally exposed population may be much smaller than the estimate reported in the dossier. The occupationally exposed population, as well as the general populations exposed to cresols, needs to be more accurately identified.

HEXACHLORO-1,3-BUTADIENE

The ITC has recommended that hexachloro-1,3-butadiene be tested for environmental effects because of evidence of widespread distribution in the aquatic environment and reports of bioaccumulation in fish and other aquatic organisms.

The supplemental literature search uncovered some information on hexachloro-1,3-butadiene toxicity to aquatic organisms and soil microfauna, on environmental fate, and on environmental occurrence. None of these reports appear to eliminate the need for the environmental effects testing recommended by the ITC.

No comments were received on the ITC's test in recommendations for hexachloro-1,3-butadiene.

PRELIMINARY APPRAISAL

The ITC's recommendation for environmental effects testing of hexachloro-1,3-butadiene seems appropriate.

NITROBENZENE

The ITC has recommended that nitrobenzene be tested for carcinogenicity, mutagenicity, and environmental effects because of its estimated annual release to the environment of 20 million pounds, its numerous dispersive uses, its ability to penetrate intact skin, and the efficiency of its absorption by inhalation.

SUPPLEMENTAL LITERATURE SEARCH

A number of articles on nitrobenzene not cited in the ITC dossier were found in the supplemental literature search. One article presented some additional data on the degradation of nitrobenzene, but the information is not considered sufficient to characterize its environmental fate.

PUBLIC COMMENTS

One comment indicated that there are test results which show that little bioaccumulation of nitrobenzene in fish has occurred. These data will need to be obtained and reviewed in detail in considering specific environmental effects testing requirements for nitrobenzene.

PRELIMINARY APPRAISAL

The ITC's recommendations for carcinogenicity, mutagenicity, and environmental effects testing of nitrobenzene seem appropriate.

TOLUENE

Over 1 million workers are thought to be exposed to toluene, which is produced in very large quantities, is used widely as a solvent and in many other ways, and has an estimated annual release rate of over 1 billion pounds. The ITC has recommended that toluene be tested for carcinogenicity, teratogenicity, and other chronic effects, and that an epidemiological study be performed on the human health effects of toluene.

SUPPLEMENTAL LITERATURE SEARCH

A number of articles were identified which presented some information on the carcinogenicity, teratogenicity, and chronic toxicity of toluene. However, the information obtained does not fill the data gaps reflected in the ITC testing recommendations.

PUBLIC COMMENTS

Comments were received which indicated that ongoing studies at the Chemical Industry Institute of Toxicology will provide information on the carcinogenicity and chronic effects, and that teratogenicity studies will follow.

EPA will review the protocols of these studies, and any available results, in detail and determine if these studies will adequately characterize these effects of toluene.

PRELIMINARY APPRAISAL

The ITC's recommendations for carcinogenicity, teratogenicity, and chronic toxicity testing of toluene seem appropriate, as does the ITC's recommendation of epidemiological study of toluene's effects on human health.

Studies in progress on carcinogencity and chronic toxicity, as well as planned studies on teratogenicity, need to be reviewed by EPA to determine whether they will adequately characerize toluene's potential to produce these effects.

XYLENES

Xylenes were recommended by the ITC for mutagenicity and teratogenicity testing, and for epidemiological study. The very large production volume and environmental release rate, the large occupationally exposed population, and widespread use in a variety of products resulting in general population exposure were noted in the ITC's recommendations.

SUPPLEMENTAL LITERATURE SEARCH

Two articles were identified in the supplemental literature search which presented some information on mutagenicity not given in the ITC dossier. However, neither study was adequate for drawing conclusions on the mutagenicity of xylenes.

PUBLIC COMMENTS

Comment 1: Initial testing should be focused on mixed xylenes rather than on testing the three xylene isomers separately. Negative results on mixed xylenes would indicate that no further testing of the individual xylenes is necessary; positive results would dictate further testing.

Response 1: EPA must, to require testing of a mixture under section 4(a), conclude that the effects of concern may not be reasonably and more efficiently determined or predicted by testing its components individually. EPA has not yet reached a conclusion on what to test in the case of xylenes. The main determinants will be the potential for additive, synergistic, or antagonistic effects and the pattern of exposure (i.e., as the mixture and as the individual xylene isomers). In addition, consideration will be given to the anticipated costs of testing the mixture versus testing the individual xylene isomers.

Comment 2: The usage of *m*-xylene (as the individual isomer) is less than 200 million pounds per year, and the production figure of 1,710 million pounds per year given in the dossier is inaccurate.

Response 2: The comment is accepted. The current production of *m*-xylene as the individual isomer appears to be about 100 million pounds per year.

PRELIMINARY APPRAISAL

The ITC's testing recommendations for xylene seem appropriate.

A critical question with respect to xylenes is whether to test the mixed xylenes, the individual isomers, or both. EPA has not yet made any judgment on this point.

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